DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

Josephine Secnik, MS, MBA
Director, Global Regulatory Affairs – U.S.
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, Indiana 46285

RE: NDA #202008
Amyvid™ (Florbetapir F 18 Injection) for intravenous use
MA #9

Dear Ms. Secnik:

As part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP), Division of Professional Drug Promotion (DPDP) of the U.S. Food and Drug Administration (FDA) has reviewed a webpage (AM77988) for Amyvid™ (Florbetapir F 18 Injection) (Amyvid), submitted by Eli Lilly and Company's (Eli Lilly) under cover of Form FDA-2253. This webpage includes a misleading multi-colored image of the brain. Additionally, OPDP has been made aware that these misleading images appeared in the commercial exhibit hall of the American Academy of Neurology annual meeting held in New Orleans, Louisiana on April 23-26, 2012. OPDP has determined that the materials misbrand Amyvid in violation of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 352(a) & (n). *See* 21 CFR 202.1(e)(6)(xviii).

Background

Below are the indication and summary of the most serious and common risks associated with the use of Amyvid.[1] According to the INDICATIONS AND USAGE section of the FDA-approved product labeling (PI):

> Amyvid is indicated for Positron Emission Tomography (PET) imaging of the brain to estimate β-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline. A negative Amyvid scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient's cognitive impairment is due to AD. A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations.

[1] This information is for background purposes only and does not necessarily represent the risk information that should be included in the promotional piece cited in this letter.

Limitations of Use:

- A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder.
- Safety and effectiveness of Amyvid have not been established for:
    - Predicting development of dementia or other neurologic condition;
    - Monitoring responses to therapies.

The PI for Amyvid contains Warnings and Precautions regarding the risk of image misinterpretation and other errors as well as the risk of radiation exposure. In addition, according to the ADVERSE REACTIONS section of the PI, the most commonly reported adverse reactions include headache, musculoskeletal pain, fatigue, and nausea.

Misleading Presentation

The Amyvid webpage features a multi-colored brain image. This presentation misleadingly suggests that Amyvid PET images can be displayed, and therefore interpreted, in color in patients with cognitive impairment who are being evaluated for Alzheimer's Disease and other causes of cognitive decline, when this is not the case. According to the DOSAGE AND ADMINISTRATION section of the PI, Amyvid PET scans should be displayed and reviewed "using a black-white scale with the maximum intensity of the scale set to the maximum intensity of all the brain pixels." The PI further includes several examples of black and white scans to illustrate proper image interpretation.

While many PET images are displayed and reviewed in color, Amyvid scans, as described above, must be displayed and reviewed using a black and white scale. Additionally, the PI does not provide instructions for estimating β-amyloid neuritic plaque density using a color scale with Amyvid. Therefore, use of the color PET scan image of a brain in Amyvid promotional materials is misleading, particularly considering the warning regarding the risk for image misinterpretation and other errors.

Conclusion and Requested Action

For the reasons discussed above, this webpage misbrands Amyvid in violation of the FD&C Act, 21 U.S.C. 352(a) & (n). *See* 21 CFR 202.1(e)(6)(xviii).

OPDP outlined its concerns about Eli Lilly's dissemination of multi-colored brain images during a June 4, 2012, teleconference. Eli Lilly replied (on June 5, 2012) with a written commitment to comply with OPDP's request to immediately cease the dissemination of these materials and any materials with the same or similar presentations for Amyvid. We appreciate this commitment and the steps that Eli Lilly has taken to address the issues outlined in this letter. Please submit a written response to this letter on or before August 24, 2012, confirming your commitment to comply with this request.

Please direct your response to the undersigned at the **Food and Drug Administration, Center for Drug Evaluation and Research, Office of Prescription Drug Promotion, Division of Professional Drug Promotion, 5901-B Ammendale Road, Beltsville,**

Maryland 20705-1266 or by facsimile at (301) 847-8444. Please note that the Division of Drug Marketing, Advertising, and Communications (DDMAC) has been reorganized and elevated to the Office of Prescription Drug Promotion (OPDP). OPDP consists of the Immediate Office, the Division of Professional Drug Promotion (DPDP) and the Division of Consumer Drug Promotion (DCDP). To ensure timely delivery of your submissions, please use the full address above and include a prominent directional notation (e.g. a sticker) to indicate that the submission is intended for OPDP. In addition, OPDP recently migrated to a different tracking system. Therefore, OPDP letters will now refer to MA numbers instead of MACMIS numbers. Please refer to MA # 9 in addition to the NDA number in all future correspondence relating to this particular matter. OPDP reminds you that only written communications are considered official.

The violations discussed in this letter do not necessarily constitute an exhaustive list. It is your responsibility to ensure that your promotional materials for Amyvid comply with each applicable requirement of the FD&C Act and FDA implementing regulations.

Sincerely,

{See appended electronic signature page}

James S. Dvorsky, PharmD
Regulatory Review Officer
Division of Professional Drug Promotion
Office of Prescription Drug Promotion

{See appended electronic signature page}

Andrew S.T. Haffer, PharmD
Acting Director
Division of Professional Drug Promotion
Office of Prescription Drug Promotion

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JAMES S DVORSKY
08/10/2012

ANDREW S HAFFER
08/10/2012